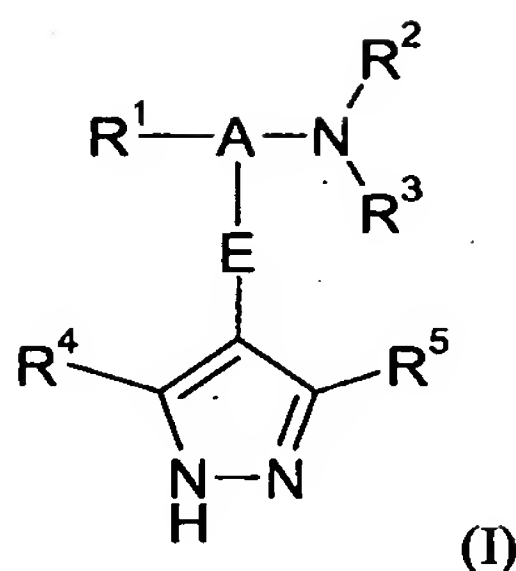


**CLAIMS**

1. A compound of the formula (I):



or a salt, solvate, tautomer or N-oxide thereof;

- 5 wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R<sup>1</sup> and NR<sup>2</sup>R<sup>3</sup> and a maximum chain length of 4 atoms extending between E and NR<sup>2</sup>R<sup>3</sup>, wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon
- 10 atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom α with respect to the NR<sup>2</sup>R<sup>3</sup> group and provided that the oxo group when present is located at a carbon atom α with respect to the NR<sup>2</sup>R<sup>3</sup> group;

- 15 E is a monocyclic or bicyclic carbocyclic or heterocyclic group wherein E is unsubstituted or has up to 4 substituents R<sup>8</sup> selected from hydroxy, oxo (when E is non-aromatic), chlorine, bromine, trifluoromethyl, cyano, C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl optionally substituted by C<sub>1-2</sub> alkoxy or hydroxyl;

- 20 R<sup>1</sup> is an aryl or heteroaryl group which is unsubstituted or bears one or more substituents selected from hydroxy; C<sub>1-4</sub> acyloxy; fluorine; chlorine; bromine; trifluoromethyl; cyano; CONH<sub>2</sub>; nitro; C<sub>1-4</sub> hydrocarbyloxy and C<sub>1-4</sub> hydrocarbyl each optionally substituted by C<sub>1-2</sub> alkoxy, carboxy or hydroxy; C<sub>1-4</sub>

acylamino; benzoylamino; pyrrolidinocarbonyl; piperidinocarbonyl;  
 morpholinocarbonyl; piperazinocarbonyl; five and six membered heteroaryl and  
 heteroaryloxy groups containing one or two heteroatoms selected from N, O and  
 S; phenyl; phenyl-C<sub>1-4</sub> alkyl; phenyl-C<sub>1-4</sub> alkoxy; heteroaryl-C<sub>1-4</sub> alkyl; heteroaryl-  
 5 C<sub>1-4</sub> alkoxy and phenoxy, wherein the heteroaryl, heteroaryloxy, phenyl,  
 phenyl-C<sub>1-4</sub> alkyl, phenyl-C<sub>1-4</sub> alkoxy, heteroaryl-C<sub>1-4</sub> alkyl, heteroaryl-C<sub>1-4</sub>  
 alkoxy and phenoxy groups are each optionally substituted with 1, 2 or 3  
 substituents selected from C<sub>1-2</sub> acyloxy, fluorine, chlorine, bromine,  
 trifluoromethyl, cyano, CONH<sub>2</sub>, C<sub>1-2</sub> hydrocarbyloxy and C<sub>1-2</sub> hydrocarbyl each  
 10 optionally substituted by methoxy or hydroxyl;

R<sup>2</sup> and R<sup>3</sup> are independently selected from hydrogen, C<sub>1-4</sub> hydrocarbyl and  
 C<sub>1-4</sub> acyl wherein the hydrocarbyl and acyl moieties are optionally substituted by  
 one or more substituents selected from fluorine, hydroxy, amino, methylamino,  
 dimethylamino and methoxy;

15 or R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are attached  
 form a cyclic group selected from an imidazole group and a saturated monocyclic  
 heterocyclic group having 4-7 ring members and optionally containing a second  
 heteroatom ring member selected from O and N;

20 or one of R<sup>2</sup> and R<sup>3</sup> together with the nitrogen atom to which they are  
 attached and one or more atoms from the linker group A form a saturated  
 monocyclic heterocyclic group having 4-7 ring members and optionally  
 containing a second heteroatom ring member selected from O and N;

or NR<sup>2</sup>R<sup>3</sup> and the carbon atom of linker group A to which it is attached  
 together form a cyano group;

25 R<sup>4</sup> is selected from hydrogen, halogen, C<sub>1-5</sub> saturated hydrocarbyl, C<sub>1-5</sub>  
 saturated hydrocarbyloxy, cyano, and CF<sub>3</sub>; and

R<sup>5</sup> is selected from hydrogen, halogen, C<sub>1-5</sub> saturated hydrocarbyl, C<sub>1-5</sub>  
 saturated hydrocarbyloxy, cyano, CONH<sub>2</sub>, CONHR<sup>9</sup>, CF<sub>3</sub>, NH<sub>2</sub>, NHCOR<sup>9</sup> or  
 NHCONHR<sup>9</sup>;

$R^9$  is a group  $R^{9a}$  or  $(CH_2)R^{9a}$ , wherein  $R^{9a}$  is a monocyclic or bicyclic group which may be carbocyclic or heterocyclic;

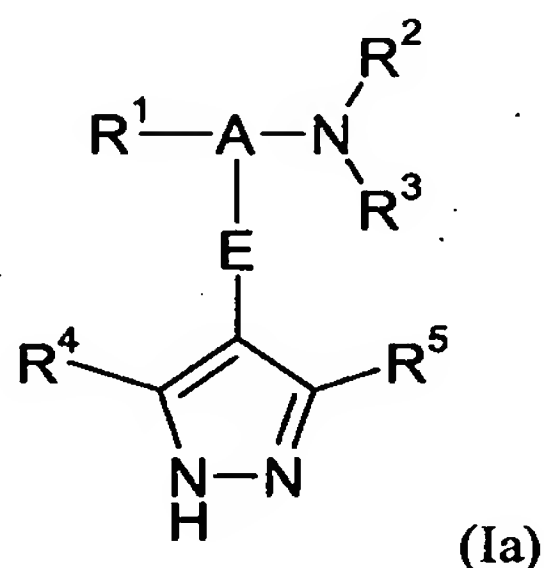
the carbocyclic group or heterocyclic group  $R^{9a}$  being optionally substituted by one or more substituents selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino; a group  $R^a-R^b$  wherein  $R^a$  is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO,  $SO_2$ ,  $NR^c$ ,  $SO_2NR^c$  or  $NR^cSO_2$ ; and  $R^b$  is selected from hydrogen, heterocyclic groups having from 3 to 12 ring members, and a  $C_{1-8}$  hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the  $C_{1-8}$  hydrocarbyl group may optionally be replaced by O, S, SO,  $SO_2$ ,  $NR^c$ ,  $X^1C(X^2)$ ,  $C(X^2)X^1$  or  $X^1C(X^2)X^1$ ;

$R^c$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl; and

$X^1$  is O, S or  $NR^c$  and  $X^2$  is =O, =S or = $NR^c$ ;

but excluding the compound (2R, 5S)-1-benzyl-4-(R)-1-(3-[1-(tert-butyl)-1,1-dimethylsilyl]oxyphenyl)-1-[4-(1H-pyrazol-4-yl)phenyl]methyl-2,5-dimethylhexahydropyrazine.

2. A compound according to claim 1 of the formula (Ia):



or a salt, solvate, tautomer or N-oxide thereof;

wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between  $R^1$  and  $NR^2R^3$  and a maximum chain length of 4 atoms extending between E and  $NR^2R^3$ , wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom  $\alpha$  with respect to the  $NR^2R^3$  group and provided that the oxo group when present is located at a carbon atom  $\alpha$  with respect to the  $NR^2R^3$  group;

E is a monocyclic or bicyclic carbocyclic or heterocyclic group wherein E is unsubstituted or has up to 4 substituents  $R^8$  as defined in claim 1;

$R^1$  is an aryl or heteroaryl group which is unsubstituted or substituted as defined in claim 1

$R^2$  and  $R^3$  are independently selected from hydrogen,  $C_{1-4}$  hydrocarbyl and  $C_{1-4}$  acyl;

or  $R^2$  and  $R^3$  together with the nitrogen atom to which they are attached form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

or one of  $R^2$  and  $R^3$  together with the nitrogen atom to which they are attached and one or more atoms from the linker group A form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

or  $NR^2R^3$  and the carbon atom of linker group A to which it is attached together form a cyano group;

$R^4$  is selected from hydrogen, halogen,  $C_{1-5}$  saturated hydrocarbyl, cyano and  $CF_3$ ; and

$R^5$  is selected from hydrogen, halogen,  $C_{1-5}$  saturated hydrocarbyl, cyano,  $CONH_2$ ,  $CONHR^9$ ,  $CF_3$ ,  $NH_2$ ,  $NHCOR^9$  or  $NHCONHR^9$ ;

$R^9$  is phenyl or benzyl each optionally substituted by one or more substituents selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino; a group  $R^a-R^b$  wherein  $R^a$  is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO,  $SO_2$ ,  $NR^c$ ,  $SO_2NR^c$  or  $NR^cSO_2$ ; and  $R^b$  is selected from hydrogen, heterocyclic groups having from 3 to 12 ring members, and a  $C_{1-8}$  hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the  $C_{1-8}$  hydrocarbyl group may optionally be replaced by O, S, SO,  $SO_2$ ,  $NR^c$ ,  $X^1C(X^2)$ ,  $C(X^2)X^1$  or  $X^1C(X^2)X^1$ ;

$R^c$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl; and

$X^1$  is O, S or  $NR^c$  and  $X^2$  is =O, =S or = $NR^c$ ;

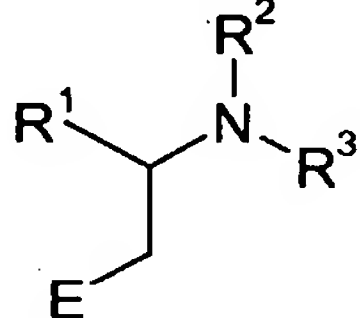
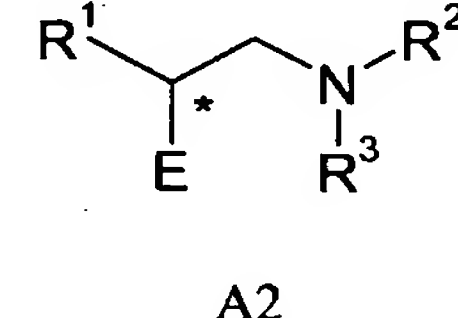
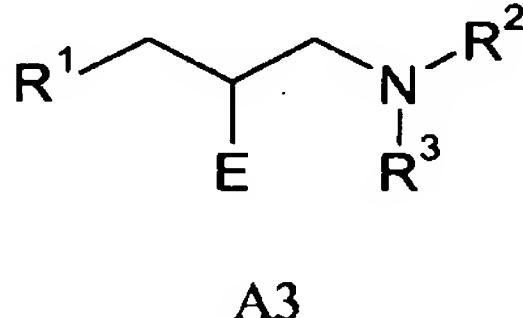
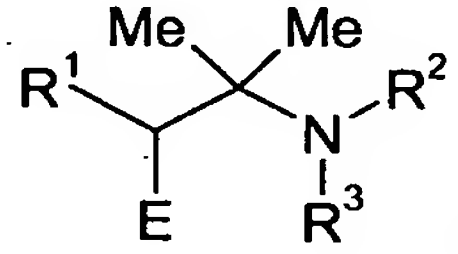
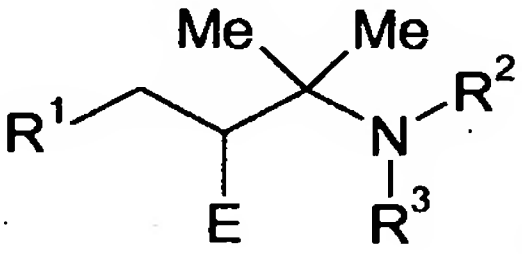
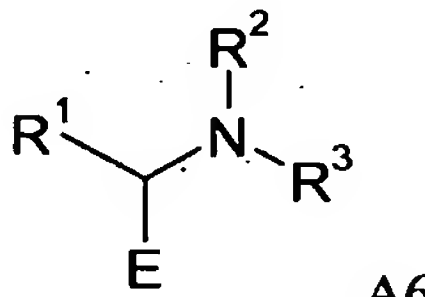
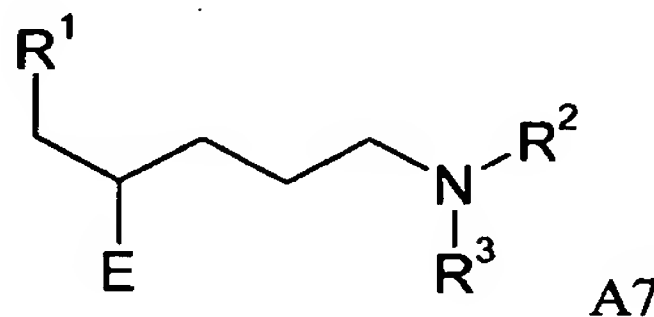
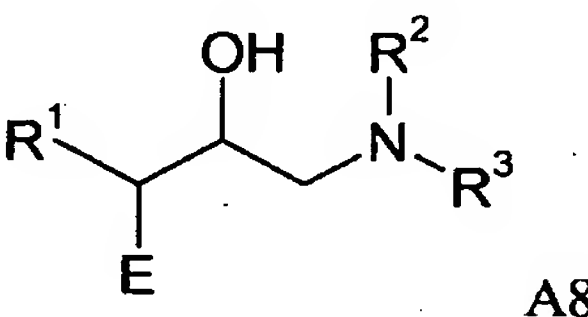
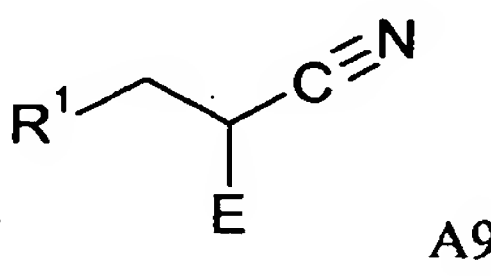
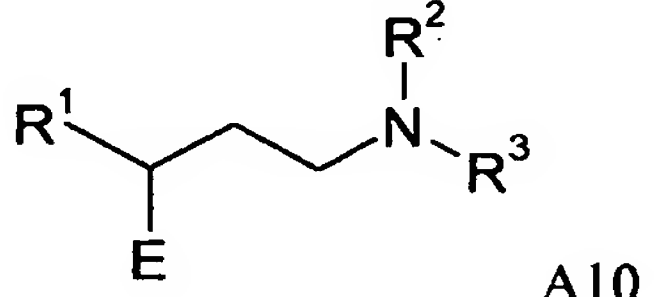
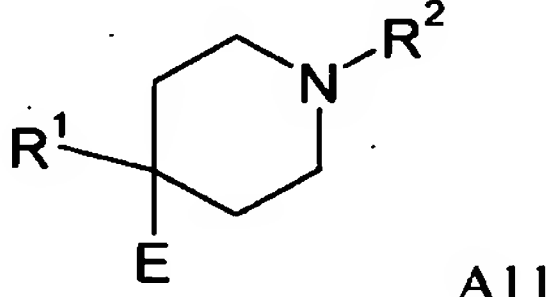
but excluding the compound (2R, 5S)-1-benzyl-4-(R)-1-(3-[1-(tert-butyl)-1,1-dimethylsilyl]oxyphenyl)-1-[4-(1H-pyrazol-4-yl)phenyl]methyl-2,5-dimethylhexahydropyrazine.

3. A compound according to claim 1 or claim 2 wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between  $R^1$  and  $NR^2R^3$  and a maximum chain length of 4 atoms extending between E and  $NR^2R^3$ , wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom  $\alpha$  with respect to the  $NR^2R^3$  group; and  $R^5$  is selected from selected from hydrogen, halogen,  $C_{1-5}$  saturated hydrocarbyl, cyano,  $CONH_2$ ,  $CF_3$ ,  $NH_2$ ,  $NHCOR^9$  and  $NHCONHR^9$ .

4. A compound according to any one of claims 1 to 3 wherein the linker group A has a maximum chain length of 3 atoms extending between  $R^1$  and  $NR^2R^3$ .

5. A compound according to claim 4 wherein the linker group A has a maximum chain length of 2 atoms extending between  $R^1$  and  $NR^2R^3$ .
6. A compound according to any one of claims 1 to 5 wherein the linker group A has a maximum chain length of 3 atoms extending between E and  $NR^2R^3$ .
- 5 7. A compound according to claim 6 wherein the linker group A has a chain length of 2 or 3 atoms extending between  $R^1$  and  $NR^2R^3$  and a chain length of 2 or 3 atoms extending between E and  $NR^2R^3$ .
8. A compound according to any one of the preceding claims wherein the linker group atom linked directly to the group E is a carbon atom and the linker group A  
10 has an all-carbon skeleton.
9. A compound according to any one of claims 1 to 7 wherein the portion  $R^1$ -A- $NR^2R^3$  of the compound is represented by the formula  $R^1$ -(G)<sub>k</sub>-(CH<sub>2</sub>)<sub>m</sub>-W-O<sub>b</sub>-(CH<sub>2</sub>)<sub>n</sub>-(CR<sup>6</sup>R<sup>7</sup>)<sub>p</sub>- $NR^2R^3$  wherein G is NH, NMe or O; W is attached to the group E and is selected from (CH<sub>2</sub>)<sub>j</sub>-CR<sup>20</sup>, (CH<sub>2</sub>)<sub>j</sub>-N and (NH)<sub>j</sub>-CH; b is 0 or 1, j is 0 or 1, k is 0 or 1, m is 0 or 1, n is 0, 1, 2, or 3 and p is 0 or 1; the sum of b and k is 0 or 1; the sum of j, k, m, n and p does not exceed 4; R<sup>6</sup> and R<sup>7</sup> are the same or different and are selected from methyl and ethyl, or CR<sup>6</sup>R<sup>7</sup> forms a cyclopropyl group; and R<sup>20</sup> is selected from hydrogen, methyl, hydroxy and fluorine.  
15
10. A compound according to any one of claims 1 to 7 wherein the moiety  $R^1$ -A- $NR^2R^3$  is represented by the formula  $R^1$ -(G)<sub>k</sub>-(CH<sub>2</sub>)<sub>m</sub>-X-(CH<sub>2</sub>)<sub>n</sub>-(CR<sup>6</sup>R<sup>7</sup>)<sub>p</sub>- $NR^2R^3$  wherein G is NH, NMe or O; X is attached to the group E and is selected from (CH<sub>2</sub>)<sub>j</sub>-CH, (CH<sub>2</sub>)<sub>j</sub>-N and (NH)<sub>j</sub>-CH; j is 0 or 1, k is 0 or 1, m is 0 or 1, n is 0, 1, 2, or 3 and p is 0 or 1, and the sum of j, k, m, n and p does not exceed 4; and R<sup>6</sup> and R<sup>7</sup> are the same or different and are selected from methyl and ethyl, or CR<sup>6</sup>R<sup>7</sup>  
20 forms a cyclopropyl group.  
25
11. A compound according to claim 10 wherein (i) k is 0, m is 0 or 1, n is 0, 1, 2 or 3 and p is 0; or (ii) k is 0, m is 0 or 1, n is 0, 1 or 2 and p is 1.

12. A compound according to claim 10 wherein (i) X is  $(\text{CH}_2)_j\text{-CH}$ , k is 1, m is 0, n is 0, 1, 2 or 3 and p is 0; or (ii) X is  $(\text{CH}_2)_j\text{-CH}$ , k is 1, m is 0, n is 0, 1 or 2 and p is 1.
13. A compound according to claim 10 or claim 12 wherein (i) j is 0; or (ii) j is 1; or (iii)  $\text{CR}^6\text{R}^7$  is  $\text{C}(\text{CH}_3)_2$ .
14. A compound according to claim 10 wherein the portion  $\text{R}^1\text{-A-NR}^2\text{R}^3$  of the compound is represented by the formula  $\text{R}^1\text{-X-(CH}_2)_n\text{-NR}^2\text{R}^3$  where X is attached to the group E and is a group CH, and n is 2.
15. A compound according to claim 1 or claim 2 wherein  $\text{R}^1\text{-A(E)-NR}^2\text{R}^3$  is selected from the groups A1 to A11 below:

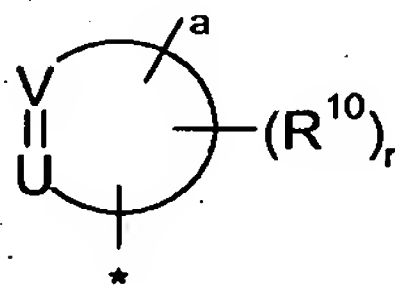
 <p>A1</p>	 <p>A2</p>	 <p>A3</p>
 <p>A4</p>	 <p>A5</p>	 <p>A6</p>
 <p>A7</p>	 <p>A8</p>	 <p>A9</p>
 <p>A10</p>	 <p>A11</p>	



16. A compound according to any one of the preceding claims wherein E is a monocyclic group.
17. A compound according to any one of the preceding claims wherein E is an aryl or heteroaryl group each of which is unsubstituted or substituted by up to 4 substituents  $R^8$  as defined in claim 1.
18. A compound according to claim 17 selected from optionally substituted phenyl, thiophene, furan, pyrimidine and pyridine groups, each of which is unsubstituted or substituted by up to 4 substituents  $R^8$  as defined in claim 1.
19. A compound according to claim 18 wherein E is a phenyl group which is unsubstituted or substituted by up to 4 substituents  $R^8$  as defined in claim 1.
20. A compound according to any one of the preceding claims wherein the group A and the pyrazole group are attached to the group E in a *meta* or *para* relative orientation; i.e. A and the pyrazole group are not attached to adjacent ring members of the group E.
21. A compound according to claim 20 wherein E is selected from 1,4-phenylene, 1,3-phenylene, 2,5-pyridylene and 2,4-pyridylene, 1,4-piperazinyl, and 1,4-piperazonyl, each of which is unsubstituted or substituted by up to 4 substituents  $R^8$  as defined in claim 1.
22. A compound according to any one of the preceding claims wherein E has 0-3 substituents.
23. A compound according to claim 22 wherein E has 0-2 substituents
24. A compound according to claim 23 wherein E has 0 or 1 substituent.
25. A compound according to claim 24 wherein E is unsubstituted.



26. A compound according to any one of the preceding claims wherein the group E is an aryl or heteroaryl group having five or six members and containing up to three heteroatoms selected from O, N and S, the group E being represented by the formula:



5

where \* denotes the point of attachment to the pyrazole group, and "a" denotes the attachment of the group A;

r is 0, 1 or 2;

U is selected from N and  $CR^{12a}$ ; and

- 10 V is selected from N and  $CR^{12b}$ ; where  $R^{12a}$  and  $R^{12b}$  are the same or different and each is hydrogen or a substituent containing up to ten atoms selected from C, N, O, F, Cl and S provided that the total number of non-hydrogen atoms present in  $R^{12a}$  and  $R^{12b}$  together does not exceed ten;

or  $R^{12a}$  and  $R^{12b}$  together with the carbon atoms to which they are attached form an unsubstituted five or six membered saturated or unsaturated ring containing up to two heteroatoms selected from O and N; and

15

$R^{10}$  is selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members; a group  $R^a-R^b$  wherein  $R^a$  is a bond, O, CO,  $X^1C(X^2)$ ,  $C(X^2)X^1$ ,  $X^1C(X^2)X^1$ , S, SO,  $SO_2$ ,  $NR^c$ ,  $SO_2NR^c$  or  $NR^cSO_2$ ; and  $R^b$  is selected from hydrogen, carbocyclic and heterocyclic groups having from 3 to 12 ring members, and a  $C_{1-8}$  hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- $C_{1-4}$  hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the  $C_{1-8}$

20

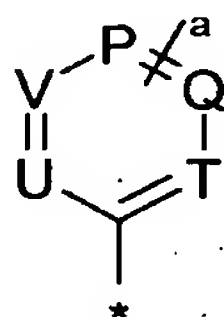
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hydrocarbyl group may optionally be replaced by O, S, SO, SO<sub>2</sub>, NR<sup>c</sup>, X<sup>1</sup>C(X<sup>2</sup>), C(X<sup>2</sup>)X<sup>1</sup> or X<sup>1</sup>C(X<sup>2</sup>)X<sup>1</sup>;

R<sup>c</sup> is selected from hydrogen and C<sub>1-4</sub> hydrocarbyl; and

X<sup>1</sup> is O, S or NR<sup>c</sup> and X<sup>2</sup> is =O, =S or =NR<sup>c</sup>.

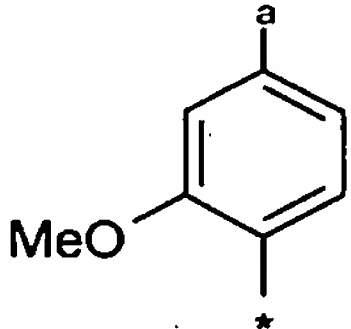
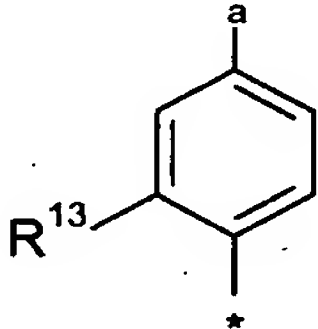
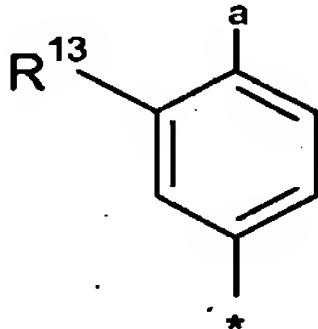
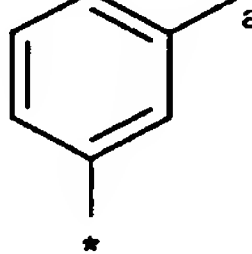
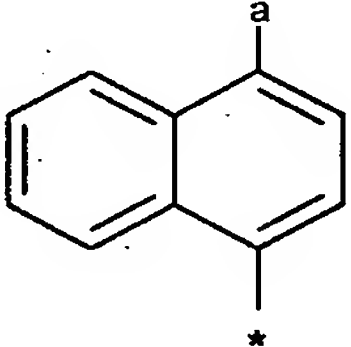
- 5 27. A compound according to claim 26 wherein E is represented by the formula:



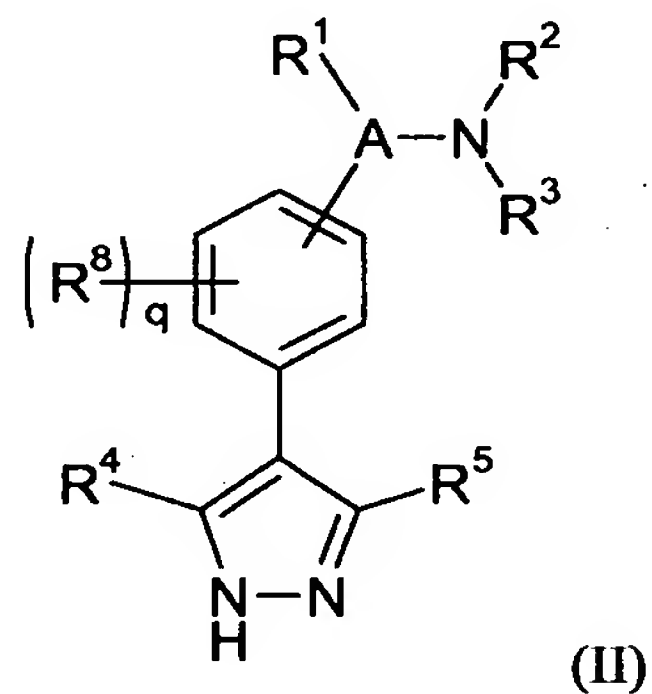
where P, Q and T are the same or different and are selected from N, CH and NCR<sup>10</sup>, provided that the group A is attached to a carbon atom.

- 10 28. A compound according to claim 27 wherein the group E is selected from groups B1 to B13 in the Table below:

<p>B1</p>	<p>B2</p>	<p>B3</p>	<p>B4</p>
<p>B5</p>	<p>B6</p>	<p>B7</p>	<p>B8</p>

 <p style="text-align: right;">B9</p>	 <p style="text-align: right;">B10</p>	 <p style="text-align: right;">B11</p>	 <p style="text-align: right;">B12</p>
 <p style="text-align: right;">B13</p>			

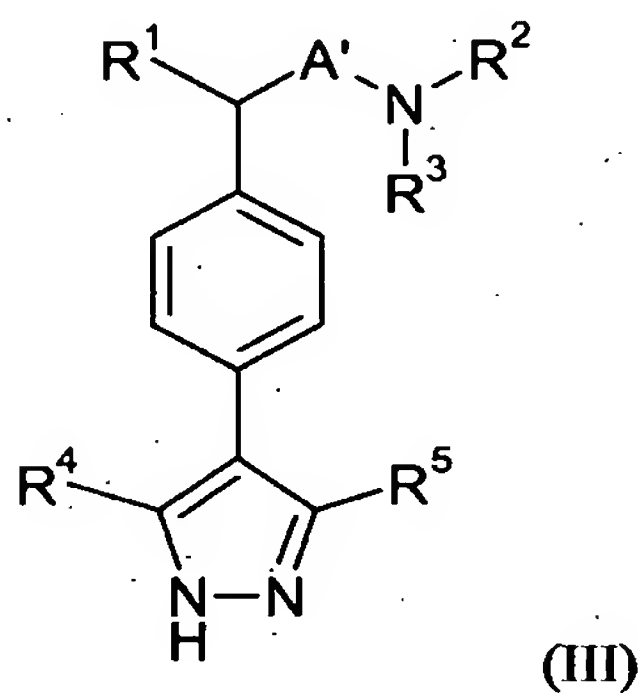
29. A compound according to claim 19 having the formula (II):



5 wherein the group A is attached to the *meta* or *para* position of the benzene ring and q is 0-4; R<sup>8</sup> is hydroxy; halogen; trifluoromethyl; cyano; C<sub>1-4</sub> hydrocarbyloxy optionally substituted by C<sub>1-2</sub> alkoxy or hydroxy; and C<sub>1-4</sub> hydrocarbyl optionally substituted by C<sub>1-2</sub> alkoxy or hydroxy.

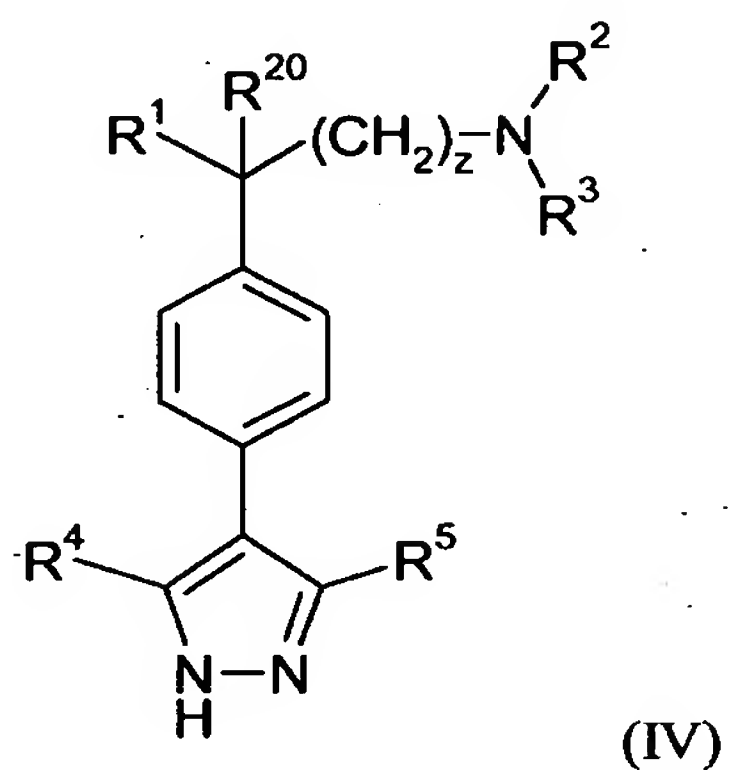
30. A compound according to claim 29 wherein q is 0, 1 or 2
31. A compound according to claim 30 wherein q is 0 or 1.

32. A compound according to claim 31 wherein q is 0.
33. A compound according to claim 19 having the formula (III):



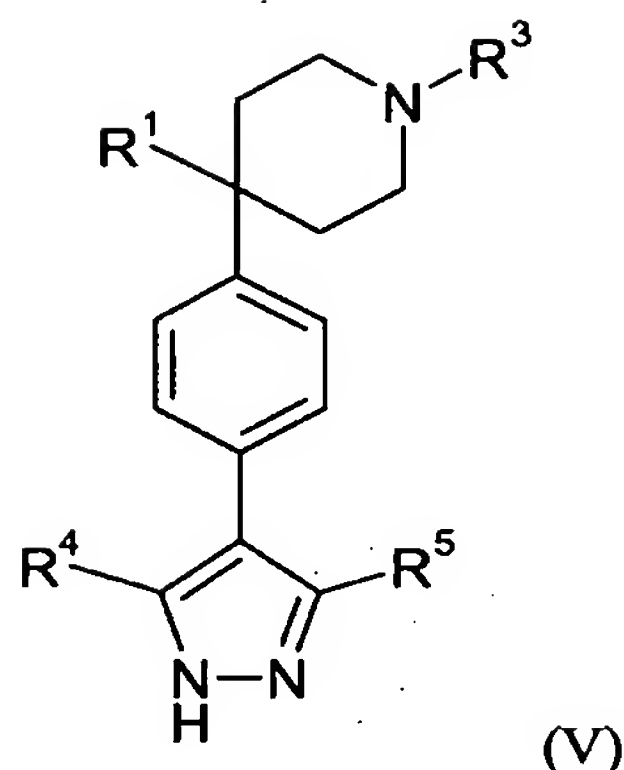
5 where A' is the residue of the group A and R<sup>1</sup> to R<sup>5</sup> are as defined in any one of the preceding claims.

34. A compound according to claim 19 having the formula (IV):



wherein z is 0, 1 or 2, R<sup>20</sup> is selected from hydrogen, methyl, hydroxy and fluorine, provided that when z is 0, R<sup>20</sup> is other than hydroxy.

- 10 35. A compound according to claim 19 having the formula (V):



wherein  $R^3$  is optionally selected from hydrogen and  $C_{1-4}$  hydrocarbyl.

36. A compound according to claim 35 wherein  $R^3$  is selected from hydrogen and  $C_{1-4}$  hydrocarbyl.
- 5 37. A compound according to claim 29 wherein  $R^1$  is phenyl.
38. A compound according to any one of the preceding claims wherein  $R^1$  is selected from phenyl, naphthyl, thienyl, furan, pyrimidine and pyridine, each optionally substituted as defined in claim 1.
- 10 39. A compound according to any one of the preceding claims wherein  $R^1$  is unsubstituted or is substituted by up to 5 substituents selected from hydroxy;  $C_{1-4}$  acyloxy; fluorine; chlorine; bromine; trifluoromethyl; cyano;  $C_{1-4}$  hydrocarbyloxy and  $C_{1-4}$  hydrocarbyl optionally substituted by  $C_{1-2}$  alkoxy or hydroxy; and five membered heteroaryl groups containing one or two heteroatoms selected from N, O and S, the heteroaryl groups being optionally substituted by one or more  $C_{1-4}$  alkyl substituents.
- 15 40. A compound according to claim 23 wherein  $R^1$  is unsubstituted or is substituted by up to 5 substituents selected from hydroxy,  $C_{1-4}$  acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano,  $C_{1-4}$  hydrocarbyloxy and  $C_{1-4}$  hydrocarbyl optionally substituted by  $C_{1-2}$  alkoxy or hydroxy.

41. A compound according to claim 23 or 24 wherein the group  $R^1$  has one or two substituents selected from fluorine, chlorine, trifluoromethyl, methyl and methoxy.
- 5 42. A compound according to claim 25 wherein  $R^1$  is a mono-chlorophenyl or dichlorophenyl group.
43. A compound according to any one of the preceding claims wherein  $R^4$  is selected from hydrogen and methyl.
- 10 44. A compound according to any one of the preceding claims wherein  $R^5$  is selected from hydrogen, fluorine, chlorine, bromine, methyl, ethyl, hydroxyethyl, methoxymethyl, cyano,  $CF_3$ ,  $NH_2$ ,  $NHCOR^{9b}$  and  $NHCONHR^{9b}$  where  $R^{9b}$  is phenyl or benzyl optionally substituted by hydroxy,  $C_{1-4}$  acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano,  $C_{1-4}$  hydrocarbyloxy and  $C_{1-4}$  hydrocarbyl optionally substituted by  $C_{1-2}$  alkoxy or hydroxy.
- 15 45. A compound according to any one of the preceding claims wherein  $R^2$  and  $R^3$  are independently selected from hydrogen,  $C_{1-4}$  hydrocarbyl and  $C_{1-4}$  acyl
46. A compound according to claim 28 wherein  $R^2$  and  $R^3$  are independently selected from hydrogen and methyl.
47. A compound according to claim 29 wherein  $R^2$  and  $R^3$  are both hydrogen.
- 20 48. A compound according to any one of the preceding claims having a molecular weight of less than 525.
- 25 49. A compound according to claim 1 of the formula (I) which is:  
 2-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 3-phenyl-2-[3-(1H-pyrazol-4-yl)-phenyl]-propionitrile;  
 2-[4-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-2-phenyl-ethylamine;  
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 2-[3-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-1-phenyl-ethylamine;

- 3-phenyl-2-[3-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 3-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 {3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 {3-(3,4-difluoro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 5 {3-(3-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propionamide;  
 3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 3-(3,4-dichloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 4-(4-chloro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 10 4-(4-methoxy-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-(4-chloro-phenyl)-1-methyl-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-phenyl-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-[4-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-4-phenyl-piperidine;  
 dimethyl-{3-[4-(1H-pyrazol-4-yl)-phenyl]-3-pyridin-2-yl-propyl}-amine;  
 15 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-dimethyl-amine;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine (R);  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine (S);  
 4-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-morpholine;  
 20 4-{4-[1-(4-chloro-phenyl)-2-pyrrolidin-1-yl-ethyl]-phenyl}-1H-pyrazole;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-isopropyl-amine;  
 dimethyl-{2-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;  
 {2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-dimethyl-amine;  
 {2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 25 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine (R);  
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine (S);  
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;  
 1-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-piperazine;  
 1-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-piperidine;  
 30 4-{4-[2-azetidin-1-yl-1-(4-chloro-phenyl)-ethyl]-phenyl}-1H-pyrazole;



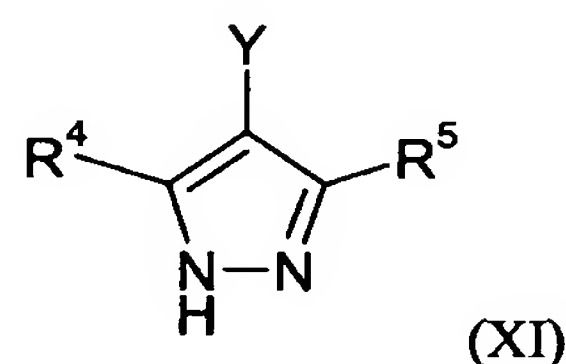
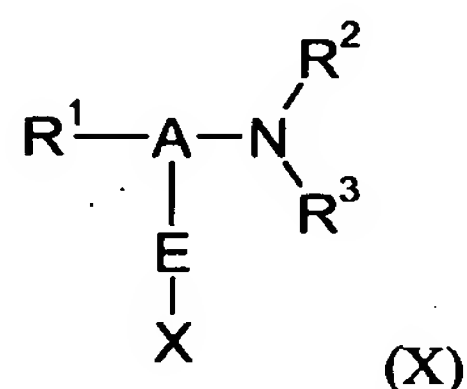
- 1-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 2-(4-chloro-phenyl)-N-methyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;  
 N-methyl-2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 5 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-ethyl-amine;  
 4-{4-[1-(4-chloro-phenyl)-2-imidazol-1-yl-ethyl]-phenyl}-1H-pyrazole;  
 methyl-{2-(4-phenoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;  
 {2-(4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 methyl-{2-[4-(pyrazin-2-yloxy)-phenyl]-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-  
 10 amine;  
 methyl-{2-phenoxy-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;  
 2-[(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methoxy}-ethylamine;  
 4-{4-[1-(4-chloro-phenyl)-3-pyrrolidin-1-yl-propyl]-phenyl}-1H-pyrazole;  
 4-{4-[3-azetidin-1-yl-1-(4-chloro-phenyl)-propyl]-phenyl}-1H-pyrazole;  
 15 methyl-{3-naphthalen-2-yl-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-amine;  
 {3-(4-fluoro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 4-{4-[4-(4-chloro-phenyl)-piperidin-4-yl]-phenyl}-1H-pyrazole-3-carbonitrile;  
 3-(4-phenoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 1-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;  
 20 1-methyl-4-{phenyl-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-[1,4]diazepane;  
 {3-(3-chloro-phenoxy)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 methyl-{2-phenyl-2-[6-(1H-pyrazol-4-yl)-pyridin-3-yl]-ethyl}-amine;  
 4-{4-[1-(4-chloro-phenyl)-3-imidazol-1-yl-propyl]-phenyl}-1H-pyrazole;  
 4-[4-(3-imidazol-1-yl-1-phenoxy-propyl)-phenyl]-1H-pyrazole;  
 25 4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenol;  
 1-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;  
 {2-(4-fluoro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 {2-(3-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 4-[4-(2-methoxy-ethoxy)-phenyl]-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 30 4-[4-(3-methoxy-propoxy)-phenyl]-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;

- 3-(3,4-dichloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propionamide;  
 2-(4-{2-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-phenoxy)-  
 isonicotinamide;  
 {2-(3-chloro-phenoxy)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;  
 5 3-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-propan-1-ol;  
 2-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-ethanol;  
 3-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-propan-1-ol;  
 2-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-ethanol;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-cyclopropylmethyl-  
 10 amine;  
 methyl-[2-[4-(1H-pyrazol-4-yl)-phenyl]-2-(4-pyridin-3-yl-phenyl)-ethyl]-amine;  
 4-{3-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-phenol;  
 3-(4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 4-(4-chloro-phenyl)-4-[4-(3-methyl-1H-pyrazol-4-yl)-phenyl]-piperidine;  
 15 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-morpholine;  
 (4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenoxy)-acetic acid;  
 4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-benzonitrile;  
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;  
 1-(4-chloro-phenyl)-2-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;  
 20 2-amino-1-(4-chloro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;  
 4-(3,4-dichloro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-(3-chloro-4-methoxy-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-(4-chloro-3-fluoro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 4-[4-(1H-pyrazol-4-yl)-phenyl]-1,2,3,4,5,6-hexahydro-[4,4']bipyridinyl;  
 25 3-(3-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 2-methylamino-1-(4-nitro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;  
 2-(3-chloro-4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 2-(4-chloro-phenyl)-2-fluoro-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 3-(3,4-dichloro-phenyl)-3-[6-(1H-pyrazol-4-yl)-pyridin-3-yl]-propylamine;  
 30 2-(4-chloro-3-fluoro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;

- 4-(2-chloro-3-fluoro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;  
 1-((3,4-dichloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl)-piperazine;  
 2-(3,4-dichloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;  
 {2-(3-chloro-4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-  
 5 amine;  
 4-{4-[2-azetidin-1-yl-1-(4-chloro-phenoxy)-ethyl]-phenyl}-1H-pyrazole;  
 3-(3-chloro-4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;  
 {3-(3-chloro-4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-  
 amine;  
 10 1-((3,4-dichloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl)-piperazine; or  
 C-(4-chloro-phenyl)-C-[4-(1H-pyrazol-4-yl)-phenyl]-methylamine;  
 and salts, solvates, tautomers and N-oxides thereof.
50. A compound according to claim 49 which is 2-amino-1-(4-chloro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol or a salt, solvate, tautomer or N-oxide thereof.
- 15 51. A compound according to any one of the preceding claims in the form of a salt, solvate, ester or N-oxide.
52. A compound as defined in any one of claims 1 to 51 for use in medicine.
53. A compound as defined in any one of claims 1 to 51 for use in (a) the prophylaxis or treatment of a disease state or condition mediated by protein kinase B; or (b)  
 20 the prophylaxis or treatment of a disease state or condition mediated by protein kinase A.
54. A compound as defined in any one of claims 1 to 51 for use in the prophylaxis or treatment of a disease state or condition which is selected from a carcinoma of the bladder, breast, colon, kidney, epidermal, liver, lung, oesophagus, gall bladder,  
 25 ovary, pancreas, stomach, cervix, endometrium, thyroid, prostate, or skin, a hematopoietic tumour of lymphoid lineage, a hematopoietic tumour of myeloid lineage, thyroid follicular cancer, a tumour of mesenchymal origin, a tumour of

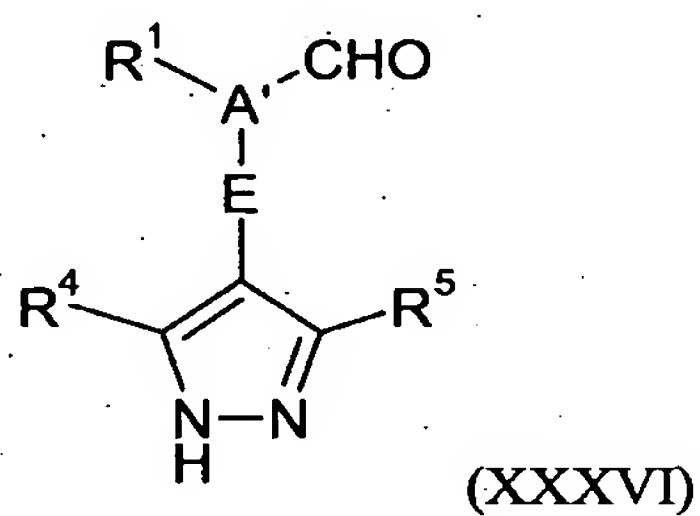
the central or peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratocanthoma, thyroid follicular cancer, or Kaposi's sarcoma.

55. A compound as defined in any one of claims 1 to 51 for use in the prophylaxis or treatment of a disease state or condition which is selected from breast cancer, ovarian cancer, colon cancer, prostate cancer, oesophageal cancer, squamous cancer and non-small cell lung carcinomas.
56. The use of a compound as defined in any one of claims 1 to 51 for:
- (a) the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by protein kinase B; or
  - (b) the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by protein kinase A; or
  - (c) the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition arising from abnormal cell growth;
  - (d) the manufacture of a medicament for the prophylaxis or treatment of a disease in which there is a disorder of proliferation, apoptosis or differentiation.
57. A pharmaceutical composition comprising a novel compound as defined in any one of claims 1 to 51 and a pharmaceutically acceptable carrier.
58. A process for the preparation of a compound of the formula (I) as defined in any one of claims 1 to 51, which process comprises:
- (a) the reaction of a compound of the formula (X) with a compound of the formula (XI) or an N-protected derivative thereof:



wherein A, E, and R<sup>1</sup> to R<sup>5</sup> are as defined in any one of claims 1 to 51, one of the groups X and Y is selected from chlorine, bromine, iodine and trifluoromethanesulphonate, and the other one of the groups X and Y is a boronate ester or boronic acid residue, in the presence of a palladium catalyst and a base;

- (b) the reductive amination of a compound of the formula (XXXVI):



with HNR<sup>2</sup>R<sup>3</sup> in the presence of a reducing agent; and optionally

- (c) the conversion of one compound of the formula (I) into another compound of the formula (I).

**European Patent Application No. 04 806 258.2**

**Astex Therapeutics Limited *et al.***

**Our Reference: 40657EP**

**Basis for amended claims in PCT application as published**

<b>Amended claim</b>	<b>Basis in PCT Appl. (PCT claims unless otherwise indicated)</b>	<b>Amended claim</b>	<b>Basis in PCT Appl.</b>
1	Claim 1 + claim 28 (R <sup>8</sup> ) + Claim 42 (R <sup>1</sup> substituents) + proviso from prior art	30	35
2	Claim 2 + claim 28 (R <sup>8</sup> ) + Claim 42 (R <sup>1</sup> substituents) + proviso from prior art	31	35
3	3	32	35
4	4	33	36
5	4	34	37 (dependency corrected)
6	5	35	38 (dependency corrected)
7	6	36	39
8	7	37	41
9	8	38	40
10	9	39	43
11	10 & 11	40	44
12	12 & 13	41	46
13	14, 15 & 16	42	47
14	17	43	48
15	18	44	49
16	21	45	50
17	22 & 28	46	51
18	23 & 28	47	52

<b>Amended claim</b>	<b>Basis in PCT Appl. (PCT claims unless otherwise indicated)</b>	<b>Amended claim</b>	<b>Basis in PCT Appl.</b>
19	24 & 28	48	54
20	26	49	55
21	27 & 28	50	55
22	29	51	56
23	29	52	76
24	29	53	57 & 65
25	30	54	Page 92 lines 6 to 21 of description
26	31	55	Page 92 lines 25 to 27 of description
27	32	56	58, 66, 67 & 68
28	33	57	75 (dependency corrected)
29	34	58	77